

# Physiological Daily Inhalation Rates for Health Risk Assessment in Overweight/Obese Children, Adults, and Elderly

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Physiological daily inhalation rates reported in our previous study for normal-weight subjects 2.6–96 years old were compared to inhalation data determined in free-living overweight/obese individuals ( $n = 661$ ) aged 5–96 years. Inhalation rates were also calculated in normal-weight ( $n = 408$ ), overweight ( $n = 225$ ), and obese classes 1, 2, and 3 adults ( $n = 134$ ) aged 20–96 years. These inhalation values were based on published indirect calorimetry measurements ( $n = 1,069$ ) and disappearance rates of oral doses of water isotopes (i.e.,  $^2\text{H}_2\text{O}$  and  $\text{H}_2^{18}\text{O}$ ) monitored by gas isotope ratio mass spectrometry usually in urine samples for an aggregate period of over 16,000 days. Ventilatory equivalents for overweight/obese subjects at rest and during their aggregate daytime activities ( $28.99 \pm 6.03$  L to  $34.82 \pm 8.22$  L of air inhaled/L of oxygen consumed; mean  $\pm$  SD) were determined and used for calculations of inhalation rates. The interindividual variability factor calculated as the ratio of the highest 99th percentile to the lowest 1st percentile of daily inhalation rates is higher for absolute data expressed in  $\text{m}^3/\text{day}$  (26.7) compared to those of data in  $\text{m}^3/\text{kg}\cdot\text{day}$  (12.2) and  $\text{m}^3/\text{m}^2\cdot\text{day}$  (5.9). Higher absolute rates generally found in overweight/obese individuals compared to their normal-weight counterparts suggest higher intakes of air pollutants (in  $\mu\text{g}/\text{day}$ ) for the former compared to the latter during identical exposure concentrations and conditions. Highest absolute mean ( $24.57 \text{ m}^3/\text{day}$ ) and 99th percentile ( $55.55 \text{ m}^3/\text{day}$ ) values were found in obese class 2 adults. They inhale on average  $8.21 \text{ m}^3$  more air per day than normal-weight adults.

**KEY WORDS:** Air pollutants; daily inhalation rates; doubly labeled water; health risk assessment; irritants; minute ventilation rates; overweight/obese subjects; ventilatory equivalent

## 1. INTRODUCTION

Health effects of inhaled environmental, occupational, and nonindustrial indoor irritants have been reported in humans.<sup>(1–16)</sup> The magnitude of the airway irritation notably depends on the water solubility

of inhaled irritants as well as the airflow-driven and locally deposited doses of these chemicals (e.g., ammonia, sulfur dioxide, ozone, and nitrogen dioxide) to the tissues within the respiratory tract.<sup>(9,17,18)</sup> The incidence of asthma among workers exposed to irritant gases has also been found to be elevated particularly in construction, textile, shoemaking, metal plating, electrical machinery, and pulp and paper industries.<sup>(12,14,15,19–23)</sup>

Prior observations indicate that overweight/obese individuals are inhaling more air per day (in  $\text{m}^3/\text{day}$ ) compared to their normal-weight subjects.<sup>(24)</sup> Consequently, the former could

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inhale more chemicals on a 24-hour basis (in  $\mu\text{g}/\text{day}$ ) compared to the latter, considering similar exposure concentrations and conditions. Obesity-related conditions are already associated with several diseases, including type 2 diabetes, insulin resistance, osteoarthritis, cardiovascular illness, asthma, sleep apnea, chronic obstructive pulmonary diseases, pulmonary embolism, and cancers.<sup>(25–29)</sup>

The doubly labeled water (DLW) method is thought to provide the most accurate data of total daily energy expenditures (TDEEs)<sup>(30–33)</sup> and daily inhalation rates,<sup>(34–36)</sup> both for free-living people of all ages and with various physiological conditions.<sup>(37–41)</sup> TDEEs encompass all energy expended by humans during real-life situations in their normal surroundings each minute of the day, 24-hours/day, on a daily basis over a long period of time—from 7 to 21 days.<sup>(31)</sup>

The classical methodology for the determination of inhalation data<sup>(24,42–44)</sup> in free-living subjects involves the multiplication of TDEE values by two central and constant values,<sup>(45)</sup> namely, the oxygen uptake factor ( $H$ ) of 0.21 L of  $\text{O}_2/\text{kcal}$  and the ventilatory equivalent (VQ) of 27 (L of air inhaled/L of oxygen consumed).  $H$  corresponds to the volume of oxygen consumed at standard temperature and pressure, dry air (STPD) to produce 1 kcal of energy expended, whereas VQ is the ratio of the minute ventilation rate (VE) at body temperature and saturated with water vapor (BTPS) to the oxygen consumption rate ( $\text{VO}_2$ ) at STPD. In Brochu *et al.*,<sup>(46)</sup> the accuracy of inhalation data (in particular, the precision of upper limits of percentiles) was improved by the determination and integration into the calculation process of mean, standard deviation ( $SD$ ), and minimal as well as maximal values for  $H$  and VQ, not only for subjects at rest ( $H_F$  and  $\text{VQ}\beta$ ) but also during their aggregate daytime activities ( $H_P$  and  $\text{VQ}\alpha$ ). Nevertheless, this improved methodology was exclusively used for the determination of daily inhalation rates in normal-weight individuals, including adults with body mass index (BMI) values ranging from 18.5 to  $<25 \text{ kg}/\text{m}^2$ . The same was applied to  $\text{VQ}\alpha$ ,  $\text{VQ}\beta$  values.

The aim of this study is to determine the percentiles of daily inhalation rates in free-living overweight/obese male and female, including obese classes 1 (i.e., BMI from 30 to  $<35 \text{ kg}/\text{m}^2$ ), 2 (i.e., BMI from 35 to  $<40 \text{ kg}/\text{m}^2$ ), and 3 (i.e., BMI  $\geq 40 \text{ kg}/\text{m}^2$ ), adults by using the methodology developed by Brochu *et al.*<sup>(46)</sup> Prior to these calculations,  $\text{VQ}\alpha$  and  $\text{VQ}\beta$  will be determined specifically for overweight/obese subjects.

## 2. METHODOLOGY

### 2.1. Study Design

Mean and percentile values of physiological daily inhalation rates (PDIRs) were determined as a function of age in overweight/obese males ( $n = 286$ ) and females ( $n = 375$ ) aged 5–96 years and compared to those reported in Brochu *et al.*<sup>(46)</sup> for normal-weight subjects. Mean values for minute energy expenditure rates ( $E$  in  $\text{kcal}/\text{min}$ ),  $\text{VO}_2$ , VE (L/min), daily inhalation rates, and physical activity levels (PAL, unitless) were also calculated for both genders in normal-weight ( $n = 408$ ) and overweight ( $n = 225$ ), as well as obese class 1 ( $n = 93$ ), class 2 ( $n = 19$ ), and class 3 adults ( $n = 22$ ) aged 20–96 years. PAL values correspond to ratios of TDEE to basal energy expenditure (BEE) values (i.e., basal metabolic rates [BMRs] expressed on a 24-hour basis). Individual data for healthy normal-weight and overweight/obese subjects were gathered and defined according to BMI cutoffs. Overweight individuals aged 5–19 years are defined as those having BMIs higher than the 85th percentile.<sup>(47,48)</sup> In adults, normal-weight, overweight (preobese), and obese classes 1 and 2 subjects are defined as those having BMIs varying from 18.5 to  $<25$ , 25 to  $<30$ , 30 to  $<35$ , and 35 to  $<40 \text{ kg}/\text{m}^2$ , respectively.<sup>(49,50,99)</sup> Adults with BMI values equal to or greater than  $40 \text{ kg}/\text{m}^2$  are classified into the class 3 obesity group. Values for  $E$ ,  $\text{VO}_2$ , VE, and PAL, as well as daily inhalation data were determined using individual DLW measurements published in the database of the IOM<sup>(98)</sup> for overweight/obese children, adults, and elderly ( $n = 661$ ) and normal-weight adults ( $n = 408$ ). Inhalation rates were expressed as absolute values ( $\text{m}^3/\text{day}$ ), as well as relative values to the body weight ( $\text{m}^3/\text{kg}\cdot\text{day}$ ) and body surface area (BSA in  $\text{m}^2$ ). Infants, toddlers, children, and teenagers are hereafter referred to collectively as children.

### 2.2. DLW Measurements

The DLW method allows the precise determination of two types of energy expenditures in the same subjects: (1) the BMR, and (2) the TDEE value. The former is calculated from the respiratory gas-exchange rates of oxygen ( $\text{O}_2$ ) and carbon dioxide ( $\text{CO}_2$ ) monitored by indirect calorimetry in subjects 40 minutes immediately after waking up.<sup>(41,51,52)</sup> During measurements of  $\text{VO}_2$  and carbon dioxide production ( $\text{VCO}_2$ ), subjects are lying at complete rest in thermoneutral conditions and have fasted

the prior 12–13 hours. Then, values for  $\text{VO}_2$  and  $\text{VCO}_2$  (L/min) are converted into BMR values (in kcal/min), which are then multiplied by 1,440 minutes in order to obtain values for the BEE (in kcal/day). The BEE value corresponds to the energy expenditure required on a 24-hour basis to maintain the minimal tissue cellular activity in order to sustain vital functions, including blood circulation, respiration, gastrointestinal, and renal processes.<sup>(53)</sup>

TDEE values encompass all daily energy expenditures of free-living people notably for their BEE, thermogenesis, physical activities, and synthetic cost of growth.<sup>(36,40,54)</sup> The latter is the energy expended to synthesize molecules that are stored in the new tissue.<sup>(54)</sup> TDEE values are based on the disappearance rates of oral doses of water isotopes (i.e.,  $^2\text{H}_2\text{O}$  and  $\text{H}_2^{18}\text{O}$ ) monitored in body fluids of subjects (usually in urine or saliva samples) over a period of 7–21 days by gas isotope ratio mass spectrometry.<sup>(31)</sup> The disappearance rate of deuterium ( $^2\text{H}$  or  $\text{D}$ ) reflects water output and that of heavy oxygen-18 ( $^{18}\text{O}$ ) corresponds to water output plus  $\text{CO}_2$  production rates because of the rapid equilibration of the body water and bicarbonate pools by carbonic anhydrase. The difference between the two disappearance rates represents the  $\text{CO}_2$  production rate, which is converted into units of energy (i.e., TDEE, in kcal/day) by using the average respiratory quotient of the diet (RQ). The RQ value may be determined by a complete diet record over the duration of the study or respiratory gas-exchange measurements ( $\text{RQ} = \text{CO}_2 \text{ produced} / \text{O}_2 \text{ consumed}$ ). The basic principles of indirect calorimetry and the DLW method are summarized in Brochu *et al.*<sup>(55)</sup> Body weight (kg), height (cm), and BMI ( $\text{kg}/\text{m}^2$ ) values complete the set of data (with BEE and TDEE) that are systematically measured in the same subjects during the DLW method. Individual data of this set of measurements are available for each subject in the database of the IOM.<sup>(98)</sup>

### 2.3. Physiological Daily Inhalation Rates

Values for the sleeping metabolic rate (SMR in kcal/min) and the  $E$  during the aggregate daytime activities ( $E\alpha$  in kcal/min) of subjects were expressed in terms of BEE, TDEE (kcal/day), and sleep durations (Sld in hour/day) by using the following equations:

$$\text{SMR} = \left[ \frac{(\text{BEE} \times F_{\text{sleep}})}{1440} \right] \quad (1)$$

$$E\alpha = \left[ \frac{\text{TDEE} - \text{BEE}}{(24 - \text{Sld}) \times 60} \right] + \left[ \frac{\text{BEE}}{1440} \right], \quad (2)$$

where 1,440 and 60 are the conversion factors from days to minutes and hours to minutes, respectively, and 24 is the number of hours in a day.

A mean correcting factor (referred to as  $F_{\text{sleep}}$ ) of  $0.988 \pm 0.083$  for the determination of SMR values by using BEE data was calculated based on heat production rates measured in sleeping overweight/obese subjects ( $n = 26$ ) by direct calorimetry compared with their awake counterparts.<sup>(56,57)</sup> Minimal and maximal  $F_{\text{sleep}}$  values of 0.847 and 1.148, respectively, were also determined and used in this study to define lower and upper limits of  $F_{\text{sleep}}$  distributions. This reduction of average heat production rates is consistent with slightly lower mean values for tidal volumes, breathing frequency rates,  $\text{VE}$ ,  $\text{VO}_2$ ,<sup>(58–61)</sup> and systolic and diastolic blood pressures as well as heart rates that have been observed in sleeping subjects in the supine position, compared with their awake counterparts.<sup>(62,63)</sup>

PDIRs (in  $\text{m}^3/\text{day}$ ) were determined by using the following equation:<sup>(46)</sup>

$$\begin{aligned} \text{PDIR} = & [(\text{SMR} \times H_F \times \text{VQ}\beta \times \text{Sld}) \\ & + (E\alpha \times H_P \times \text{VQ}\alpha) \times (24 - \text{Sld})] \\ & \times 0.06, \end{aligned} \quad (3)$$

where  $H_F$  is the oxygen uptake factor during the fasting phase (L of  $\text{O}_2/\text{kcal}$ ),  $H_P$  is the oxygen uptake factor during the postprandial phase (L of  $\text{O}_2/\text{kcal}$ ),  $\alpha$  is the data for the aggregate daytime activities of subjects, and  $\beta$  is the data for subjects under resting conditions.

The value for  $H_F$  of  $0.2057 \pm 0.0018$  L of  $\text{O}_2/\text{kcal}$  (mean  $\pm$   $SD$ ;  $n = 31$ ) required for the combustion of metabolic fuels in fasting subjects (i.e., glycogen, glucose, 3-hydroxybutyric acid, acetoacetic acid, and triacylglycerol) has been determined by Brochu *et al.*<sup>(46)</sup> with minimal and maximal values of 0.198 L of  $\text{O}_2/\text{kcal}$  and 0.214 L of  $\text{O}_2/\text{kcal}$ , respectively. The  $H_P$  value of  $0.2059 \pm 0.0019$  L of  $\text{O}_2/\text{kcal}$  (mean  $\pm$   $SD$ ;  $n = 1,245$ ) has been calculated for the combustion of carbohydrates, proteins, and fats in subjects during the postprandial phase with minimum and maximum of 0.199 L of  $\text{O}_2/\text{kcal}$  and 0.221 L of  $\text{O}_2/\text{kcal}$  of energy expended, respectively.<sup>(46)</sup> Both  $H$  values were determined by a specific methodology developed by Brochu *et al.*<sup>(46)</sup> based on published sets of  $\text{VO}_2$  and  $\text{VCO}_2$  data measured by indirect calorimetry at STPD in the same subjects.

VQ $\beta$  and VQ $\alpha$  values (i.e., VE/VO $_2$  ratios, L of air inhaled/L of oxygen consumed) were determined in this study for each age group by gathering published sets of simultaneous measurements of VE and VO $_2$  with VO $_2$  demands within the span of VO $_2\beta$  or VO $_2\alpha$  values specific to overweight/obese subjects. These spans of VO $_2\beta$  and VO $_2\alpha$  values were preliminary calculated by using BEE and TDEE values measured in overweight/obese individuals using the following equations:<sup>(46)</sup>

$$\text{VO}_{2\beta} = \left[ \frac{\text{BEE}}{1440} \right] \times H_F \quad (4)$$

$$\text{VO}_{2\alpha} = \left[ \frac{(\text{TDEE} - \text{BEE})}{(24 - \text{Sld}) \times 60} + \frac{\text{BEE}}{1440} \right] \times H_P. \quad (5)$$

Published VO $_2$  and VCO $_2$  values were generally measured using paramagnetic O $_2$  and infrared CO $_2$  analyzers, respectively,<sup>(64)</sup> whereas published VE data were measured by spirometry or pneumotacography.<sup>(65)</sup> Values for Sld in this study ( $n = 14,732$ ) were taken from Brochu *et al.*<sup>(46)</sup> These data, resulting from a critical analysis of the literature, have been recorded day by day on questionnaires by survey respondents for periods of time ranging from 1 to 3 years with complementary data, such as body weight (kg), height (cm), and BMI values (in kg/m $^2$ ) of respondents and those regarding work conditions, physical activities, diet, as well as health and socioeconomic variables.<sup>(66–69)</sup>

PDIR values (in m $^3$ /day) were expressed per unit of BSA (in m $^2$ ) using the formula developed by Mosteller<sup>(70)</sup> based on height (cm) and body weight (Bw in kg) values:<sup>(70)</sup>

$$\text{BSA} = \left[ \frac{\text{height} \times \text{Bw}}{3600} \right]^{0.5}. \quad (6)$$

This equation is preferentially recommended for accurate BSA calculations in children<sup>(71,72)</sup> and adults<sup>(73)</sup> compared to other algorithms.<sup>(74–81)</sup>

Mean values for  $E\alpha$  (kcal/min), VO $_2\beta$ , and VO $_2\alpha$  (L/min) in normal-weight, overweight, and obese classes 1, 2, and 3 adults were calculated by using Equations (2), (4), and (5), respectively, whereas those for  $E\beta$  (in kcal/min) and VE $\beta$  (in L/min) in fasting subjects at rest, as well as VE $\alpha$  (in L/min) during the postprandial phase, were determined by using the following equations:

$$E\beta = \left[ \frac{\text{BEE}}{1440} \right] \quad (7)$$

$$\text{VE}\beta = \left[ \frac{\text{BEE}}{1440} \right] \times H_F \times \text{VQ}\beta \quad (8)$$

$$\text{VE}\alpha = \left[ \frac{(\text{TDEE} - \text{BEE})}{(24 - \text{Sld}) \times 60} + \frac{(\text{BEE})}{1440} \right] \times H_P \times \text{VQ}\alpha. \quad (9)$$

## 2.4. Statistical Analysis

Data were grouped by age, usually with more than 30 subjects per group in order to optimize the probability of achieving a normal distribution for each age group, as formally recommended according to the central limit theorem.<sup>(82–84)</sup> Anderson-Darling goodness-of-fit tests were carried out on individual TDEE, BEE, body weight, and BSA values, per age group, in order to determine their best fit distribution (i.e., lognormal or normal). The best fit distributions for Sld,  $H_P$ ,  $H_F$ , VQ $\beta$ , and VQ $\alpha$  values were taken from Brochu *et al.*<sup>(46)</sup> Mean and *SD* values as well as distribution percentiles were calculated for daily inhalation rates. Monte Carlo simulations were necessary to integrate *SD* values of input data into the calculation process of parameters of interest (i.e., VQ $\beta$ , VQ $\alpha$ , VO $_2\beta$ , VO $_2\alpha$ , VE $\beta$ , VE $\alpha$ , and PDIR). They were conducted based on random sampling involving 10,000 iterations for each calculation process. For each age group, statistical differences in mean values between normal-weight and overweight/obese individuals have been calculated by using the Mann-Whitney test (data not shown in tables).

## 3. RESULTS

Mean and *SD* values for body weight, BSA, BMI, BEE, and TDEE data as well as results of Anderson-Darling goodness-of-fit tests appear in Table I. Mean, *SD*, and distribution percentiles for VQ $\beta$  and VQ $\alpha$  values are reported in Tables II and III, respectively. Mean, *SD*, and percentiles for PDIRs in overweight/obese males and females aged 5–96 years old are presented in Tables IV and V, respectively. Mean body weight, BSA, BEE, TDEE,  $E\beta$ ,  $E\alpha$ , PAL, VO $_2\beta$ , VO $_2\alpha$ , VE $\beta$ , and VE $\alpha$  values as well as PDIRs in normal-weight, overweight, and classes 1, 2, and 3 obese adults aged 20–96 years old are reported in Table VI.

Mean and percentile inhalation data expressed per unit of body weight (in m $^3$ /kg-day) in overweight/obese subjects are higher in children than

**Table 1.** Anthropometric and Energetic Measurements in Healthy Overweight/Obese Males and Females Aged 5–96 Years

Gender and Age Group (years)	n	Body Weight (kg)		Body Surface Area (m <sup>2</sup> )		BMI <sup>a</sup> (kg/m <sup>2</sup> )	Energetic Measurements (kcal/day)							
		Mean ± SD	B	Mean ± SD	B		BEE <sup>b</sup>			TDEE <sup>c</sup>				
							Mean ± SD	Min	Max	Mean ± SD	Min	Max		
Males														
5 to <7	68	27.2 ± 4.7	L	0.94 ± 0.09	L	19.7 ± 2.60	1,177 ± 113	965	1,470	L	1,673 ± 251	1,122	2,741	L
7 to <10	27	40.1 ± 10.0	L	1.22 ± 0.18	L	21.4 ± 3.30	1,374 ± 190	1,101	1,928	L	2,141 ± 473	1,386	3,341	L
10 to <16.5	26	58.1 ± 10.6	N	1.54 ± 0.16	N	26.5 ± 4.73	1,659 ± 207	1,320	2,155	N	2,496 ± 298	1,878	3,096	L
16.5 to <35	21	106.9 ± 23.5	L	2.17 ± 0.30	L	29.2 ± 8.03	2,024 ± 246	1,649	3,035	L	3,490 ± 435	2,646	4,704	L
35 to <45	45	98.1 ± 20.1	L	2.20 ± 0.24	L	30.6 ± 5.38	1,953 ± 304	1,463	2,916	L	3,636 ± 653	2,438	5,139	L
45 to <65	38	97.0 ± 16.6	L	2.17 ± 0.21	L	31.2 ± 4.61	1,818 ± 260	1,410	2,474	L	3,378 ± 634	2,337	4,610	L
65 to ≤96	61	85.0 ± 10.9	L	2.02 ± 0.16	L	28.4 ± 2.77	1,687 ± 230	1,298	2,588	L	2,605 ± 470	1,831	3,837	L
Females														
5 to <7	65	28.0 ± 6.5	L	0.95 ± 0.13	L	20.0 ± 3.13	1,113 ± 137	830	1,490	L	1,564 ± 236	1,104	2,516	L
7 to <10	57	39.2 ± 10.5	L	1.20 ± 0.19	L	21.7 ± 4.15	1,242 ± 153	1,028	1,630	L	1,969 ± 362	1,211	2,699	N
10 to <16.5	58	60.9 ± 12.7	N	1.61 ± 0.21	N	25.5 ± 3.74	1,492 ± 175	1,071	1,920	N	2,469 ± 482	1,599	3,581	N
16.5 to <35	57	83.0 ± 8.8	L	1.94 ± 0.19	L	29.8 ± 4.82	1,544 ± 124	1,243	1,993	L	2,740 ± 328	1,613	3,609	N
35 to <45	27	93.8 ± 21.2	L	2.08 ± 0.24	L	33.6 ± 7.10	1,677 ± 281	1,267	2,576	L	2,942 ± 421	2,357	4,391	L
45 to <65	61	82.0 ± 15.1	L	1.92 ± 0.19	L	30.9 ± 5.74	1,408 ± 178	1,080	1,860	N	2,243 ± 375	1,276	3,255	N
65 to ≤96	50	71.4 ± 10.6	L	1.77 ± 0.16	L	28.2 ± 2.90	1,293 ± 165	910	1,845	L	1,902 ± 361	1,017	3,091	L

Note: N = normal; L = lognormal; n = number of individuals; SD = standard deviation.

<sup>a</sup>BMI = body mass index. BMI cutoffs for overweight individuals were higher than the 85th percentile for subjects aged 5–19 years and varying from 25 kg/m<sup>2</sup> to 30 kg/m<sup>2</sup> for adults over 19 years of age. Adults over 19 up to 96 years were considered to be obese when their BMIs were greater than 30 kg/m<sup>2</sup>. (48–50,99)

<sup>b</sup>BEE = basal energy expenditure (i.e., basal metabolic rate expressed on a 24-hour basis) measured by indirect calorimetry. (98)

<sup>c</sup>TDEE = total daily energy expenditure. TDEEs were based on <sup>2</sup>H<sub>2</sub>O and H<sub>2</sub><sup>18</sup>O disappearance rates from urine monitored by gas isotope ratio mass spectrometry during 7–21-day periods for free-living individuals. (98)

B = best-fitting distribution (i.e., lognormal or normal) according to the Anderson-Darling goodness-of-fit test performed on individual data for each age group.



**Table II.** Ventilatory Equivalent Ratios ( $VO_2\beta$ ) for Healthy Overweight/Obese Individuals Aged 4–96 Years at Rest

Ventilatory Equivalent Ratios ( $VO_2\beta^b$ , L of air inhaled/L of oxygen consumed)																		
Age Groups <sup>a</sup> (years)	<i>n</i>	Mean $\pm$ SD	Min	Max	Ref <sup>c</sup>	Percentiles											$VO_2\beta^d$ (L/min)	
						1st	2.5nd	5th	10th	25th	50th	75th	90th	95th	97.5th	99th	Min	Max
4 to <10	16	32.11 $\pm$ 7.71	23.80	50.05	A	23.98	24.19	24.70	25.51	28.13	31.85	37.03	41.93	44.88	46.60	48.67	0.123	0.290
10 to <16.5	107	30.99 $\pm$ 3.76	23.71	46.57	B	24.32	24.87	25.53	26.31	28.33	30.69	33.40	35.92	37.59	39.17	40.68	0.161	0.324
16.5 to <35	96	33.91 $\pm$ 15.20	18.00	100.51	C	18.36	18.94	19.85	21.56	25.46	32.67	42.07	55.83	64.55	69.87	79.87	0.175	0.442
35 to <45	49	34.81 $\pm$ 7.41	22.06	91.46	D	23.07	23.87	24.84	26.46	29.88	34.23	39.46	45.01	48.82	52.85	55.71	0.176	0.420
45 to $\leq$ 96	62	31.38 $\pm$ 3.51	22.23	43.18	E	24.03	25.02	25.75	26.51	28.59	30.89	33.54	36.23	37.48	39.06	40.07	0.128	0.369

Notes: TDEE and BEE (in kcal/day) are defined in Table I.  $H_F$  and Sld values are taken from Brochu *et al.*<sup>(46)</sup>  $n$  = number of individuals; SD = standard deviation; min = minimal value; max = maximal value.

<sup>a</sup>For both genders.

<sup>b</sup> $VO_2\beta$  = ratio of the minute ventilation rate ( $VE\beta$  in L/min at BTSP) to the oxygen uptake ( $VO_2\beta$  in L/min at STPD).

<sup>c</sup>The simultaneous  $VE\beta$  and  $VO_2\beta$  measurements used for VQ calculations were taken from the following studies: A, <sup>(101,102)</sup> B, <sup>(101,103,104)</sup> C, <sup>(101,105–114)</sup> D, <sup>(101,106,111–113,115–117)</sup> E, <sup>(101,109,111–113,118–120)</sup>.

<sup>d</sup> $VO_2\beta$  =  $[BEE/(1,440)] \times H_F$ , where  $H_F$  = oxygen uptake factor in fasting subjects.  $H_F$  =  $0.2057 \pm 0.0018$  L of  $O_2$ /kcal.

**Table III.** Ventilatory Equivalent Ratios ( $VO_2\alpha$ ) During the Aggregate Daytime Activities of Healthy Overweight/Obese Individuals Aged 4–96 Years

Ventilatory Equivalent Ratios ( $VO_2\alpha^b$ , L of air inhaled/L of oxygen consumed)																		
Age Groups <sup>a</sup> (years)	<i>n</i>	Mean $\pm$ SD	Min	Max	Ref <sup>c</sup>	Percentiles											$VO_2\alpha^d$ (L/min)	
						1st	2.5nd	5th	10th	25th	50th	75th	90th	95th	97.5th	99th	Min	Max
4 to <10	44	30.86 $\pm$ 3.91	21.29	50.05	F	22.73	23.51	24.83	25.83	28.17	30.58	33.41	36.21	37.73	39.64	40.86	0.128	0.789
10 to <16.5	116	28.99 $\pm$ 6.03	16.08	50.84	G	17.66	19.42	20.56	22.17	24.87	28.66	32.73	36.75	39.18	42.09	44.74	0.221	0.795
16.5 to <35	170	31.01 $\pm$ 12.47	15.71	100.51	H	16.07	16.79	17.95	19.38	23.36	29.42	37.35	47.10	53.99	59.95	68.61	0.221	1.074
35 to <45	50	34.82 $\pm$ 8.22	19.92	91.46	I	20.60	21.91	23.69	25.60	28.89	33.92	39.77	46.51	51.47	54.95	59.60	0.334	1.058
45 to $\leq$ 96	85	31.92 $\pm$ 3.31	22.31	46.15	J	25.12	26.12	26.81	27.77	29.50	31.60	33.85	36.30	37.35	38.44	40.28	0.104	0.922

Notes: TDEE and BEE (in kcal/day) are defined in Table I.  $H_P$  and Sld values are reported in Brochu *et al.*<sup>(46)</sup>  $n$  = number of individuals; SD = standard deviation; min = minimal value; max = maximal value.

<sup>a</sup>For both genders.

<sup>b</sup> $VO_2\alpha$  = ratio of the minute ventilation rate ( $VE\alpha$  in L/min at BTSP) to the oxygen uptake ( $VO_2\alpha$  in L/min at STPD).

<sup>c</sup>The simultaneous  $VE\alpha$  and  $VO_2\alpha$  measurements used for  $VO_2\alpha$  calculations were taken from the following studies: F, <sup>(101,102,121,122)</sup> G, <sup>(101,103,123–125)</sup> H, <sup>(101,105–114,123,126–131)</sup> I, <sup>(106,107,111–113,117,126,127,132,133)</sup> J, <sup>(101,109,111–113,118–120,126)</sup>.

<sup>d</sup> $VO_2\alpha$  =  $[(TDEE-BEE)/((24-Sld) \times 60) + BEE/(1,440)] \times H_P$ , where  $H_P$  = postprandial oxygen uptake factor.  $H_P$  =  $0.2059 \pm 0.0019$  L of  $O_2$ /kcal. Sld = sleep duration (in hours/day).

**Table IV.** Distribution Percentiles of Physiological Daily Inhalation Rates for Overweight/Obese Males Aged 5–96 Years

Physiological Daily Inhalation Rates <sup>a</sup>												
Age Group (years)	Mean ± SD	Percentiles										
		1st	2.5nd	5th	10th	25th	50th	75th	90th	95th	97.5th	99th
		(m <sup>3</sup> /day)										
5 to <7	10.86 ± 1.94	6.76	7.49	8.05	8.57	9.54	10.64	12.07	13.38	14.19	15.09	16.03
7 to <10	13.84 ± 3.12	8.14	8.81	9.54	10.21	11.61	13.32	15.78	18.03	19.57	21.22	22.97
10 to <16.5	15.02 ± 2.77	9.96	10.45	11.05	11.69	13.04	14.74	16.66	18.70	20.05	21.57	22.65
16.5 to <35	23.35 ± 7.80	11.91	12.84	13.84	15.14	17.87	21.90	26.92	33.15	38.30	42.90	50.55
35 to <45	26.34 ± 6.83	14.82	16.24	17.07	18.27	21.36	25.58	30.33	35.02	38.51	41.88	47.52
45 to <65	21.97 ± 4.00	14.51	15.09	15.90	16.96	18.97	21.60	24.63	27.49	29.25	30.43	32.24
65 to ≤96	17.00 ± 3.09	11.33	11.84	12.40	13.18	14.76	16.66	19.00	21.15	22.30	23.58	25.24
(m <sup>3</sup> /kg-day) <sup>b</sup>												
5 to <7	0.408 ± 0.099	0.224	0.245	0.270	0.290	0.335	0.399	0.470	0.537	0.578	0.629	0.681
7 to <10	0.354 ± 0.111	0.166	0.192	0.204	0.224	0.276	0.340	0.411	0.497	0.564	0.618	0.667
10 to <16.5	0.260 ± 0.063	0.148	0.160	0.172	0.186	0.215	0.252	0.294	0.344	0.381	0.404	0.442
16.5 to <35	0.228 ± 0.091	0.091	0.103	0.114	0.133	0.164	0.212	0.272	0.342	0.397	0.467	0.512
35 to <45	0.269 ± 0.086	0.121	0.144	0.161	0.172	0.206	0.254	0.316	0.381	0.425	0.481	0.537
45 to <65	0.228 ± 0.054	0.131	0.139	0.149	0.162	0.188	0.223	0.260	0.301	0.328	0.349	0.378
65 to ≤96	0.199 ± 0.042	0.118	0.127	0.140	0.149	0.169	0.194	0.224	0.257	0.278	0.290	0.313
(m <sup>3</sup> /m <sup>2</sup> -day) <sup>b</sup>												
5 to <7	11.66 ± 2.34	7.15	7.81	8.15	8.83	10.01	11.49	13.03	14.69	15.68	16.50	17.93
7 to <10	11.51 ± 3.09	6.21	6.59	7.26	7.94	9.29	11.12	13.29	15.57	17.30	19.20	20.83
10 to <16.5	9.84 ± 2.04	6.01	6.48	6.94	7.36	8.41	9.62	11.05	12.62	13.51	14.51	15.52
16.5 to <35	10.43 ± 3.66	4.95	5.46	5.96	6.68	7.95	9.70	12.08	15.22	17.49	19.64	21.93
35 to <45	11.98 ± 3.33	6.41	6.89	7.48	8.11	9.62	11.51	13.83	16.31	17.91	19.39	22.19
45 to <65	10.12 ± 2.01	6.21	6.68	7.12	7.59	8.64	10.02	11.42	12.77	13.67	14.47	15.48
65 to ≤96	8.36 ± 1.63	5.38	5.68	5.99	6.33	7.13	8.17	9.37	10.52	11.23	11.86	12.63

<sup>a</sup>Daily inhalation rates =  $[(\text{SMR} \times H_F \times \text{VOQ} \times \text{Sld}) + (E\alpha \times H_P \times \text{VOQ}\alpha) \times (24\text{-Sld})] \times 0.06$ , and  $\text{SMR} = [\text{BEE} \times F_{\text{sleep}}]/1,440$ .  $E\alpha = [(\text{TDEE-BEE})/(24\text{-Sld}) \times 60] + \text{BEE}/1,440$ . BEE and TDEE (kcal/day) are defined and given in Table I.  $\text{VOQ}\beta$  and  $\text{VOQ}\alpha$  (unitless) are reported in Tables II and III. Sld (hours/day) and  $H_P$  as well as  $H_F$  values were taken from Brochu *et al.*<sup>(46)</sup> SMR = sleeping metabolic rate (kcal/min).  $H_F$  and  $H_P$  = oxygen uptake factor during fasting and postprandial phases, respectively, (L of O<sub>2</sub>/kcal).  $H_F = 0.2057 \pm 0.0018$  L/kcal, min. = 0.198 L/kcal, max. = 0.214 L/kcal.  $H_P = 0.2059 \pm 0.0019$  L/kcal, min. of 0.199 L/kcal, max. of 0.221 L/kcal.  $F_{\text{sleep}}$  is a correcting factor of BEE values.  $F_{\text{sleep}} = 0.995 \pm 0.070$ , min. = 0.847, max. = 1.148.

<sup>b</sup>Daily inhalation rates were divided by body weights and body surface areas reported in Table I in order to obtain values expressed in m<sup>3</sup>/kg-min and m<sup>3</sup>/m<sup>2</sup>-min, respectively. SD = standard deviation, min = minimum, max = maximum.

**Table V.** Distribution Percentiles of Physiological Daily Inhalation Rates for Overweight/Obese Females Aged 5–96 Years

Physiological Daily Inhalation Rates <sup>a</sup>												
Age Group (years)	Mean ± SD	Percentiles										
		1st	2.5nd	5th	10th	25th	50th	75th	90th	95th	97.5th	99th
		(m <sup>3</sup> /day)										
5 to <7	10.18 ± 1.80	6.57	7.06	7.60	7.94	8.87	10.03	11.27	12.57	13.31	14.00	14.89
7 to <10	12.70 ± 2.42	7.44	7.95	8.56	9.43	11.01	12.69	14.26	15.69	16.84	17.66	18.33
10 to <16.5	15.15 ± 3.51	8.80	9.55	10.14	11.05	12.46	14.71	17.24	19.78	21.84	23.06	24.84
16.5 to <35	18.18 ± 6.03	8.92	9.83	10.79	11.86	13.71	17.00	21.23	25.96	28.77	32.69	37.68
35 to <45	21.57 ± 5.08	12.58	13.66	14.53	15.84	17.78	20.93	24.41	28.02	30.91	33.42	36.91
45 to <65	14.63 ± 2.66	9.14	9.72	10.41	11.30	12.71	14.45	16.37	18.20	19.31	20.08	21.06
65 to ≤96	12.32 ± 2.53	7.33	8.10	8.56	9.27	10.51	12.11	13.89	15.62	16.68	18.18	19.30
(m <sup>3</sup> /kg-day) <sup>b</sup>												
5 to <7	0.372 ± 0.099	0.193	0.207	0.229	0.253	0.301	0.360	0.429	0.502	0.550	0.594	0.647
7 to <10	0.335 ± 0.098	0.153	0.168	0.197	0.217	0.263	0.323	0.398	0.470	0.508	0.548	0.590
10 to <16.5	0.254 ± 0.078	0.128	0.140	0.150	0.165	0.197	0.239	0.297	0.363	0.407	0.444	0.478
16.5 to <35	0.221 ± 0.079	0.101	0.112	0.122	0.135	0.166	0.207	0.264	0.327	0.366	0.414	0.459
35 to <45	0.228 ± 0.068	0.114	0.122	0.135	0.149	0.178	0.219	0.271	0.318	0.348	0.386	0.419
45 to <65	0.182 ± 0.045	0.099	0.104	0.116	0.128	0.149	0.176	0.211	0.243	0.259	0.276	0.295
65 to ≤96	0.175 ± 0.044	0.093	0.103	0.112	0.124	0.144	0.170	0.200	0.233	0.255	0.273	0.307
(m <sup>3</sup> /m <sup>2</sup> -day) <sup>b</sup>												
5 to <7	10.75 ± 2.25	6.41	6.95	7.38	7.98	9.20	10.60	12.11	13.70	14.70	15.61	17.17
7 to <10	10.69 ± 2.49	5.81	6.38	6.94	7.67	8.88	10.49	12.20	13.98	15.14	16.11	17.14
10 to <16.5	9.51 ± 2.45	5.36	5.75	6.10	6.68	7.67	9.11	10.88	12.98	14.08	15.08	16.79
16.5 to <35	9.37 ± 3.20	4.31	5.02	5.35	5.99	7.08	8.77	10.98	13.62	15.13	16.97	19.40
35 to <45	10.32 ± 2.58	5.75	6.11	6.76	7.31	8.43	9.98	11.80	13.70	15.01	16.42	17.33
45 to <65	7.65 ± 1.54	4.63	5.00	5.26	5.71	6.51	7.55	8.62	9.77	10.36	10.94	11.69
65 to ≤96	6.97 ± 1.53	3.97	4.35	4.77	5.13	5.94	6.81	7.88	8.87	9.84	10.58	11.12

<sup>a</sup>Daily inhalation rates =  $[(\text{SMR} \times H_F \times \text{VOQ} \times \text{Sld}) + (E\alpha \times H_P \times \text{VOQ}) \times (24 - \text{Sld})] \times 0.06$ , and  $\text{SMR} = [\text{BEE} \times F_{\text{sleep}}]/(1,440 \times E\alpha) = [(\text{TDEE} - \text{BEE})/((24 - \text{Sld}) \times 60)] + \text{BEE}/1,440$ . BEE and TDEE (kcal/day) are defined and given in Table I. VOQ and VOQ $\alpha$  (unitless) are reported in Tables II and III. Sld (hours/day) and  $H_P$  as well as  $H_F$  values were taken from Brochu *et al.*<sup>(46)</sup> SMR = sleeping metabolic rate (kcal/min).  $H_F$  and  $H_P$  = oxygen uptake factor during fasting and postprandial phases, respectively (L of O<sub>2</sub>/kcal).  $H_F = 0.2057 \pm 0.0018$  L/kcal, min = 0.198 L/kcal, max = 0.214 L/kcal.  $H_P = 0.2059 \pm 0.0019$  L/kcal, min of 0.199 L/kcal, max of 0.221 L/kcal.  $F_{\text{sleep}}$  is a correcting factor of BEE values.  $F_{\text{sleep}} = 0.995 \pm 0.070$ , min = 0.847, max = 1.148.

<sup>b</sup>Daily inhalation rates were divided by body weights and body surface areas reported in Table I in order to obtain values expressed in m<sup>3</sup>/kg-min and m<sup>3</sup>/m<sup>2</sup>-min, respectively. SD = standard deviation. min = minimum, max = maximum.



**Table VI.** Anthropometric and Inhalation Data in Healthy Adults Aged 20 to 96 Years as a Function of Body Mass Index Values

Classification of Adult Overweight and Obesity According to BMI Cutoffs						
Anthropometric and Inhalation Data for Both Genders	Units	Normal-weight ( <i>n</i> = 408)	Overweight ( <i>n</i> = 225)	Obese class 1 ( <i>n</i> = 93)	Obese class 2 ( <i>n</i> = 19)	Obese class 3 ( <i>n</i> = 22)
		Mean ± <i>SD</i>	Mean ± <i>SD</i>	Mean ± <i>SD</i>	Mean ± <i>SD</i>	Mean ± <i>SD</i>
BMI <sup>a</sup> span	(kg/m <sup>2</sup> )	18.5 to < 25	25.0 to <30	30.0 to <35	35.0 to < 40	≥ 40.0
Body weight	(kg)	63.52 ± 2.41	78.04 ± 2.46	91.83 ± 2.46	111.76 ± 2.13	130.20 ± 4.02
Body surface area	(m <sup>2</sup> )	1.73 ± 0.04	1.91 ± 0.04	2.08 ± 0.04	2.32 ± 0.03	2.46 ± 0.05
BEE <sup>b</sup>	(kcal/day)	1,439 ± 60	1,544 ± 59	1,670 ± 53.1	2,022 ± 55	1,955 ± 52
TDEE <sup>b</sup>	(kcal/day)	2,456 ± 136	2,611 ± 150	2,883 ± 125.6	3,582 ± 157	3,167 ± 115
E $\beta$ <sup>c</sup>	(kcal/min)	1.00 ± 0.04	1.07 ± 0.04	1.16 ± 0.04	1.41 ± 0.04	1.36 ± 0.04
E $\alpha$ <sup>c</sup>	(kcal/min)	2.08 ± 0.15	2.21 ± 0.17	2.44 ± 0.14	3.03 ± 0.17	2.63 ± 0.12
PAL <sup>d</sup>	(unitless)	1.71 ± 0.12	1.69 ± 0.12	1.73 ± 0.09	1.77 ± 0.10	1.62 ± 0.07
VO <sub>2</sub> $\beta$ fasting phase <sup>e</sup>	(L/min)	0.205 ± 0.009	0.220 ± 0.009	0.238 ± 0.008	0.289 ± 0.008	0.279 ± 0.008
VE $\beta$ fasting phase <sup>c</sup>	(L/min)	6.22 ± 0.43	7.34 ± 0.93	7.91 ± 0.84	9.86 ± 1.34	9.38 ± 1.12
VE $\alpha$ <sup>c</sup>	(L/min)	14.21 ± 1.81	14.76 ± 2.21	16.46 ± 2.09	20.60 ± 3.12	17.80 ± 2.33
Physiological daily inhalation rates <sup>e</sup>	(m <sup>3</sup> /day)	16.36 ± 1.68	17.54 ± 2.14	19.51 ± 2.06	24.57 ± 3.12	21.51 ± 2.32
	(m <sup>3</sup> /kg-day)	0.259 ± 0.03	0.224 ± 0.028	0.211 ± 0.023	0.219 ± 0.028	0.164 ± 0.018
	(m <sup>3</sup> /m <sup>2</sup> -day)	9.47 ± 1.00	9.14 ± 1.139	9.33 ± 1.00	10.54 ± 1.35	8.64 ± 0.93

<sup>a</sup>BMI = body mass index.

<sup>b</sup>BEE and TDEE for overweight/obese adults (kcal/day) are defined and given in Table I.

<sup>c</sup>E = minute energy expenditure rate, VO<sub>2</sub> = oxygen consumption rate, VE = minute ventilation rate,  $\beta$  = data under resting conditions,  $\alpha$  = data for the aggregate daytime activities.  $E\beta = BEE/1,440$ .  $E\alpha = [(TDEE-BEE)/(24-Sld) \times 60] + BEE/1,440$ .  $VO_2\beta = (BEE/1,440) \times H_F$ .  $VO_2\alpha = [(TDEE-BEE)/(24-Sld) \times 60] + BEE/1,440 \times H_P$ .  $VE\beta = (BEE/1,440) \times H_F \times VQ\beta$ .  $VE\alpha = [(TDEE-BEE)/(24-Sld) \times 60] + BEE/1,440 \times H_P \times VQ\alpha$ . H = oxygen uptake factor (L of O<sub>2</sub>/kcal). H during fasting (*H<sub>F</sub>*) and postprandial (*H<sub>P</sub>*) phases as well as VQ $\beta$  and VQ $\alpha$  values for overweight/obese adults are defined and given in Tables II and III. BEE, TDEE, VQ $\beta$ , and VQ $\alpha$  values for normal-weight adults (kcal/day) were taken from Brochu *et al.*<sup>(46)</sup>

<sup>d</sup>PAL = physical activity level (TDEE/BEE ratio).

<sup>e</sup>Daily inhalation rates = [(SMR  $\times$  H<sub>F</sub>  $\times$  VQ $\beta$   $\times$  Sld) + (E $\alpha$   $\times$  H<sub>P</sub>  $\times$  VQ $\alpha$ )  $\times$  (24-Sld)]  $\times$  0.06, and SMR = [BEE  $\times$  F<sub>sleep</sub>]/1,440. SMR = sleeping metabolic rate (kcal/min). F<sub>sleep</sub> is a correcting factor of BEE values. F<sub>sleep</sub> in overweight/obese individuals = 0.995  $\pm$  0.070. F<sub>sleep</sub> in normal-weight subjects = 0.960  $\pm$  0.023.<sup>(46)</sup> Sld values (i.e., sleep duration in hours/day) were taken from Brochu *et al.*<sup>(46)</sup> SD = standard deviation.

in adults (Tables IV and V). The same applies in most cases when males are compared to females. These data are usually lower than those reported in Brochu *et al.*<sup>(46)</sup> for normal-weight subjects. For instance, the 99th percentile of 0.667 m<sup>3</sup>/kg-day for overweight/obese males aged 7–9 years old is 7% lower than the value of 0.712 m<sup>3</sup>/kg-day for normal-weight boys of same age. Overweight/obese boys and girls aged 5 to <10 years are generally inhaling more air per unit of BSA (in m<sup>3</sup>/m<sup>2</sup>-day) than overweight/obese adults. Finally, the comparison between normal-weight and overweight/obese inhalation percentile and mean values expressed in m<sup>3</sup>/m<sup>2</sup>-day does not follow a clear tendency. For instance, the mean of 9.14 m<sup>3</sup>/m<sup>2</sup>-day in normal-weight adults is 4%, 2%, and 10% higher than values for overweight, obese class 1, and obese class 3 adults, respectively, and 11% lower than the one for obese class 2 adults (Table VI).

Daily inhalation means in adults aged 20–96 years (Table VI) are gradually increasing when BMI values increase from 18.5 up to <40 kg/m<sup>2</sup>, but slightly decrease when BMI are greater than 40 kg/m<sup>2</sup>. These inhalation data are consistent with the corresponding increasing mean values for BEE, TDEE, PAL (i.e., TDEE/BEE ratio), and body weight, respectively, for these groups of subjects (Table VI). Obese class 3 subjects were physically less active (PAL of 1.62, VO<sub>2α</sub> of 0.542 L/min, VE<sub>α</sub> of 17.80 L/min) than obese class 2 individuals (PAL 1.77, VO<sub>2α</sub> of 0.632 L/min, VE<sub>α</sub> of 20.60 L/min). Despite a relatively high mean BEE value (1,955 kcal/day), the lower mean TDEE value for the former (3,167 kcal/day), compared to the one for the latter (3,582 kcal/day), has required a lower oxygenation rate on a 24-hour basis, and, of course, a lower mean daily inhalation rate (21.51 m<sup>3</sup>/day compared to 24.57 m<sup>3</sup>/day). Obese class 3 and class 2 adults are inhaling an average of 5.15 m<sup>3</sup> and 8.21 m<sup>3</sup> more air per day, respectively, than their normal-weight counterparts, in order to be adequately oxygenated. The highest 99th percentile of 55.55 m<sup>3</sup>/day was found in obese class 2 males compared to the one of 31.89 m<sup>3</sup>/day reported in Brochu *et al.*<sup>(46)</sup> for normal-weight subjects.

#### 4. DISCUSSION

The integration of mean and *SD* values for VQ<sub>β</sub> and VQ<sub>α</sub> determined in this study (Tables II and III) as well as *H<sub>F</sub>* and *H<sub>P</sub>* data (taken from Brochu *et al.*<sup>(46)</sup>) into the calculation process

of inhalation rates has allowed the determination of upper limits of percentiles in overweight/obese children, adults, and elderly that never have been estimated before (Tables IV and V). Some overweight/obese individuals inhale more air on a daily basis (thus more air pollutants) than would be expected from past observations in people of different body weight categories, including normal-weight, overweight, and obese subjects.<sup>(24)</sup> For instance, values for 99th percentiles calculated in this study for overweight/obese children 10 to <16.5 years and adults 35 to <45 years (22.64–24.84 m<sup>3</sup>/day and 36.91–47.52 m<sup>3</sup>/day, respectively) by using mean and *SD* values for *H<sub>F</sub>*, *H<sub>P</sub>*, VQ<sub>β</sub>, and VQ<sub>α</sub> are higher than highest 99th percentiles that have been calculated in one of our studies<sup>(24)</sup> published in 2006 for children (19.13 m<sup>3</sup>/day) and adults (28.81 m<sup>3</sup>/day) in the same body weight category based on DLW measurements and central *H* and VQ data. The same applies for percentiles expressed per unit of body weight. For instance, 99th percentiles reported in this study for girls and boys aged from 5 to <7 years of age of 0.647 and 0.681 m<sup>3</sup>/kg-day, respectively, are higher than the highest 99th percentile of 0.526 m<sup>3</sup>/kg-day published in Brochu *et al.*<sup>(24)</sup> for overweight/obese children. Some inhalation percentiles in overweight/obese subjects are also higher than the estimate of 20 m<sup>3</sup>/day adopted by the Federal Register for a 70-kg adult.<sup>(85)</sup> For instance, values between 75th and 99th percentiles in males aged 16.5 to <35 years, 35 to <45 years, 45 to <65 years old varying from 26.92 to 50.55 m<sup>3</sup>/day, 30.33 to 47.52 m<sup>3</sup>/day, and 24.63 to 32.24 m<sup>3</sup>/day, respectively, are 1.3–2.5-, 1.5–2.4-, and 1.2–1.6-fold higher than the Federal Register value of 20 m<sup>3</sup>/day.<sup>(85)</sup> Moreover, in girls and boys aged 5 to <10 years old, 75–99th percentiles expressed per kg of weight (0.398–0.647 m<sup>3</sup>/kg-day and 0.411–0.681 m<sup>3</sup>/kg-day, respectively) are 1.4–2.3- and 1.4–2.4-fold higher than the Federal Register value of 0.286 m<sup>3</sup>/kg-day.<sup>(85)</sup>

Means of absolute PDIRs (in m<sup>3</sup>/day) calculated in this study for overweight/obese subjects are higher than those reported in Brochu *et al.*<sup>(46)</sup> for normal-weight individuals, when age groups are similar (Tables IV and V). Overweight/obese males are inhaling on average 1.8–6.2 m<sup>3</sup> of extra volumes of air per day (i.e., 11–31% more air per day) than their normal-weight counterparts. This comparison excludes age groups of boys 10 years to <16.5 years old that were statistically different by 27% (*p* < 0.05). Gaps between overweight/obese and

normal-weight mean rates in females aged 5 to <45 years and 45–96 years range from 1.6 m<sup>3</sup>/day to 5.4 m<sup>3</sup>/day (i.e., by 12.8–33.1%) and 0.2 m<sup>3</sup>/day to 0.8 m<sup>3</sup>/day (i.e., by 1.1–7.1%), respectively. Most absolute percentiles (in m<sup>3</sup>/day) gathered per age groups in overweight/obese subjects (i.e., 60 of 77 in females; 60 of 66 in males, excluding boys aged 10 years to <16.5 years; Tables IV and V) are higher than those for normal-weight individuals. For instance, highest 99th percentiles of 27.90 m<sup>3</sup>/day and 35.40 m<sup>3</sup>/day for normal-weight females and males, respectively,<sup>(46)</sup> are exceeded by the following percentiles determined in overweight/obese subjects 16.5 to <45 years of age: 97.5th and 99th percentiles varying from 28.77 m<sup>3</sup>/day to 37.68 m<sup>3</sup>/day in females and 95th, 97.5th, and 99th percentiles ranging from 38.3 m<sup>3</sup>/day to 50.55 m<sup>3</sup>/day in males (Tables IV and V).

Human interindividual variability factors in inhalation data (expressed per m<sup>3</sup>/day, m<sup>3</sup>/kg-day, and m<sup>3</sup>/m<sup>2</sup>-day) were calculated for entire cohorts ( $n = 1,896$ ) of normal-weight individuals 2.6 months to 96 years of age reported in Brochu *et al.*<sup>(46)</sup> and overweight/obese subjects 5–96 years old included in this study. The magnitude of human variability in inhalation data as reflected by lowest 1st percentiles of 1.89 m<sup>3</sup>/day, 0.093 m<sup>3</sup>/kg-day, and 3.79 m<sup>3</sup>/m<sup>2</sup>-day (data not showed in tables of Brochu *et al.*<sup>(46)</sup>) and highest 99th percentiles of 50.55 m<sup>3</sup>/day, 1.138 m<sup>3</sup>/kg-day, and 22.29 m<sup>3</sup>/m<sup>2</sup>-day, respectively, correspond to factors of 26.7, 12.2, and 5.9 (classified in the same order). The adequacy of the default uncertainty factor or the human kinetic adjustment factor (HKAF) currently used in health risk assessment can be assessed as the ratio of the highest 95th percentile to the lowest 50th percentile of internal doses in cohorts of subjects exposed to air pollutants.<sup>(134–136)</sup> Therefore, interindividual variability factors were also calculated as the ratio of highest 95th percentiles to lowest 50th percentiles of inhalation data. Consequently, interindividual variability factors of 11.1, 5.5, and 2.7 were calculated as the ratio of highest 95th percentiles of 38.51 m<sup>3</sup>/day, 0.937 m<sup>3</sup>/kg-day, and 18.44 m<sup>3</sup>/m<sup>2</sup>-day to lowest 50th percentiles of 3.47 m<sup>3</sup>/day, 0.170 m<sup>3</sup>/kg-day, and 6.81 m<sup>3</sup>/m<sup>2</sup>-day, respectively.

#### 4.1. Accuracy of Input Data

Inhalation data in this study were calculated by using body weight, height, BEE, and TDEE values that have been systematically measured in the same subjects by the DLW method. Values for BEE were obtained by indirect calorimetry measurements ( $n = 1,069$ ), whereas those for TDEE were derived

from gas isotope ratio mass spectrometry analysis of disappearance rates of oral doses of deuterium (<sup>2</sup>H) and heavy oxygen-18 (<sup>18</sup>O) for an aggregate period of over 16,000 days. The accuracy of BEE values derived from indirect calorimetry measurements has been shown to vary from +1% to +2%.<sup>(86)</sup> The mean precision of TDEE values ranges from –1.0% to +3.3% when the sources of drinking water are not changed during the period of DLW studies.<sup>(31)</sup> Mean errors of –8.7% in infants and +5.3% in soldiers on TDEE values were observed when the sources of tap water were modified.<sup>(87,88)</sup> In the worst-case scenario, simultaneous minimal and maximal mean errors associated with energetic input parameters (i.e., BEE and TDEE) and  $H$  values were shown to have a combined effect varying from –3.0% to +2.3% on the accuracy of PDIRs.<sup>(46)</sup> This span of potential errors on inhalation values (i.e., –3.0% to +2.3%) is insignificant compared to those based on time-activity-ventilation, food-energy intakes, metabolic equivalents, and parameter  $A$  approaches, which vary from –49% to +122% for some 24-hour breathing estimates.<sup>(43)</sup>

The possible shorter Sld values in overweight/obese children and adults compared to their normal-weight counterparts<sup>(89–92,100)</sup> was found to have a negligible influence on the order of magnitude of daily inhalation rates.<sup>(46)</sup> A 25% decrease in Sld data for 60% of overweight/obese children, 35% of overweight adults, and 55% of their obese counterparts (i.e., the worst-case scenario according to the literature) has decreased the global PDIRs of entire cohorts of subjects by only 0.03–0.17%.<sup>(46)</sup> Some publications also suggest that sleep duration in subjects is inversely related to BMI increases.<sup>(69,93–95)</sup> Overall, what precedes has justified the use in this study of Sld values gathered by Brochu *et al.*<sup>(46)</sup> from the literature regardless of the under-, normal-weight, overweight, and obese proportions of individuals in the different cohorts.

## 5. CONCLUSION

Based on absolute means and percentiles of PDIRs (in m<sup>3</sup>/day), many overweight/obese individuals, in particular obese class 2 and class 3 adults, are expected to inhale more air pollutants (thus more irritants) on a 24-hour basis (i.e., in µg/day) compared to their normal-weight counterparts during identical exposure concentrations and conditions. Inhalation rates per units of body weight (in m<sup>3</sup>/kg-day) and BSA (in m<sup>3</sup>/m<sup>2</sup>-day) in overweight/obese

children and adults will lead to generally higher intakes of air pollutants (i.e., in  $\mu\text{g}/\text{kg}\cdot\text{day}$  and  $\mu\text{g}/\text{m}^2\cdot\text{day}$ , respectively) for the former compared to the latter. The same applies when males are compared to females. The integration into the calculation process of BEE and TDEE data with mean, *SD*, minimal, and maximal values for subjects at rest ( $H_F$  and  $VQ\beta$ ) and during their aggregate daytime activities ( $H_P$  and  $VQ\alpha$ ) has assured mean potential errors on inhalation data varying from  $-3.0\%$  to  $+2.3\%$ . The determination of minute ventilation rates during the aggregate daytime activities of overweight/obese adults are recommended in future studies, notably for use in occupational risk assessments. The adequacy of the default uncertainty factor or the HKAF currently used in health risk assessment<sup>(96,97)</sup> should be assessed based on individual variability factors calculated in this study for inhalation data (i.e., 2.7–26.7) along with the variability of other pharmacokinetic determinants.

## DECLARATION OF INTEREST

The authors report no declarations of interest.

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